(a) a container having therein a first population of reagent red blood cells bearing group A antigen and a second population of reagent red blood cells bearing B antigen, wherein one of the populations of reagent red blood cells is stained;

(b) reaction means for carrying out the reverse ABO blood type; and

(c) instructions for performing the reverse ABO blood type, wherein the column is subjected to visual or automated computerized imaging analysis.

Cl 46 cont

47. The kit of claim 46 wherein the reaction means for performing the reverse ABO blood type is selected from the group consisting of tube, microplate, slide, slide platform and column agglutination technology.

48. The kit of claim 47 wherein the reaction means for carrying out the reverse ABO blood type is a column agglutination test reaction vessel.

49. The method of claim 16 wherein the sample of blood is serum or plasma.

50. The method of claim 25 wherein the sample of blood is serum or plasma.

51. The method of claim 31 wherein the sample of blood is serum or plasma.

REMARKS

Claims 16, 20, 22, 23, and 25-51 are pending in the application and have been rejected. After this Amendment, claims 16, 20, 22, 23, and 25-51 remain in this case. It is respectfully submitted that the amended

claims are fully supported in the specification as filed and that no new matter has been added.

The amendments have been made pursuant to the requirements of Rule 121 of the Rules of Practice. Specifically, the pending claims as amended are written above in clean form and in accordance with 37 C.F.R. § 1.121(c)(1)(i) and § 1.121(c)(3). Pursuant to the requirements of 37 C.F.R.§ 1.121(c)(1)(ii), another version of the amended claims is attached hereto as Exhibit A. This Exhibit A1-A4 version has been marked up to show all changes made in this amendment relative to the previous version of each claim and the specification where amended. As stated hereinabove, the amendments do not constitute new matter. Entry and consideration of the amendments is therefore respectfully requested.

The Examiner has required Applicant to submit acceptable corrected drawings. Applicants herein have so submitted the formal drawings.

Rejection under 35 U.S.C. §112 first paragraph

Claims 16, 20, 22, 23 and 25-51 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention.

In particular, the Examiner avers that claims 16, 20, 29, 22, 23 and 49 positively claim identical subject matter as claimed in claims 25, 26, 30, 27, 28 and 50, respectively, and differ only in the intended use recitations of their preambles, which the Examiner avers do not serve to distinguish the same subject matter from

itself. The Examiner further avers that in these claims it is not clear what is encompassed or excluded by "in a single test" because a single test may be a multi-vessel technology.

Applicants traverse this rejection as to the alternative claiming rejection in that Applicants should be able to claim their invention alternatively, here wherein the preamble of 25 makes it a narrower version of that of claim 16. Both sets of claims are supported in the specification, see for example page 9, line 27 to page 11, line 16. It is respectfully submitted that the specification contemplates not only ABO typing but multiple antigen typing for example determination of antigens D, C, E, c, e, M, N, S, s, P_1, Le^a, Le^b, K, k, Js^a, Fy^a, Fy^b, Jk^a, Jk^b, Lu^a, and Lu^b antigens, and the like (see specification at page 24, lines 10-21 and in particular see page 24 lines 14-16). Another example of a method for analyzing blood in a reverse test is in any binding ligand test, and in particular in an antibody screen. See specification at page 5, line 24 to page 6, line 6; and page 24, line 23 to page 25, line 8. Both sets of claims should be acceptable and thus Applicants respectfully request that both sets of claims 16, 20, 29, 22, 23 and 49 and 25, 26, 30, 27, 28 and 50, should be patentable.

Applicants have amended independent claims 16 and 25 to make clear that the test is performed in a *single column*. Such testing is thus done without the need for a confirmatory test. Support for this amendment is found in the original specification at page 23, lines 13-18, Example 2 Part C lines at page 31, lines 13-14, and Table 6.

The Examiner further avers that in claims 25-28, 30 and 50, it is not clear what is being determined because the relationship of the cell populations to reverse ABO typing is not clear as reverse ABO typing is accepted as determining antibodies not cell populations.

Applicants have amended independent claim 25 to recite "A method of determining reverse ABO type in a sample using two cell populations in a single column". It is respectfully submitted that such amendment clarifies that which is the subject of the test (a blood sample, not cell populations). Support for this amendment is found in the specification at Example 2 Part C lines at page 31, lines 13-14, and Table 6. Since claims 26-28, 30 and 50 depend on amended claim 25, it is respectfully submitted that the amendment to claim 25 will remove the rejection with regard to the remaining dependent claims.

The Examiner further avers that in claims 31-35 and 51, it is not clear what is being determined because the relationships of antibody testing to the cell populations and to reverse ABO type are not clear; and that in these claims it is not clear what is encompassed or excluded by "in a single test" because a single test may be a multi-vessel technology.

Applicants have amended independent claim 31 to recite that Applicants are claiming "A method of simultaneous blood antibody testing of a blood sample using two cell populations . . ."; and to make clear that the test is performed in a single column. Such testing is thus done without the need for a confirmatory test.

Support for these amendments is found in the original specification at page 23, lines 13-18, Example 2 Part C lines at page 31 lines 13-14, and Table 6. Since claims 32-35 and 51 depend on amended claim 31, it is respectfully submitted that the amendment to claim 31 will remove the rejection with regard to the remaining dependent claims.

The Examiner further avers that in claims 36-41 the interrelationships of the steps and components are not clear, for example because: the relationship of antibody to sample or admixture is not clear; the relationship of antibody to first or second antigen or to agglutinate is not clear; the relationship of screen to detecting and identifying is not clear, that in these claims it is not clear what is encompassed or excluded in a "single test" because a single test may be a multi-vessel technology.

Applicants have amended claim 36 to specify that the invention in this embodiment is "A method of performing an antibody test on a sample of blood in a single column . . .". As stated in the specification, the antibody can be any blood contained antibody, such as those elaborated at page 24, lines 10-21 and in particular see specification at page 24, lines 14-16. Applicants have stated in the specification that an antibody test can be performed in a single column using the reverse testing methods disclosed. In relevant part, the specification at page 24, line 23 to page 25, line 8, states the following:

> The methods of the invention have been illustrated in great detail for use in a blood serology context. However, it should be understood that it is within the contemplation of the invention to conduct simultaneous forward and reverse type binding assays involving any binding ligands associated with

particles, such that the particles will react as a result of the binding of the ligands to their binding partners in both a forward and reverse fashion. For example, the "antibody screen" test, which is routinely performed using plasma or serum that has been separated from the sample RBC's, could be performed using whole blood with labeled reagent red cells used as disclosed here. Alternatively, serum or plasma could be used but the number of tests required to perform an antibody screen or antibody identification could be reduced by 50% by mixing 1 unlabeled reagent red cell and 1 labeled reagent red cell. Although red blood cell forward and reverse typing system is illustrated, one skilled in the art will appreciate that other systems may be optimized in this manner.

Applicants thus seek to claim a method of performing an antibody screen using a reverse test method as disclosed.

The Examiner further avers that in claims 42-45, "the populations" and "the antibody" lack antecedent basis. Applicants have amended independent claim 42 to recite "a container having therein a first population of reagent red blood cells bearing a first antigen and a second population of reagent red blood cells bearing a second antigen,", thus removing the rejection to lack of antecedent basis for "the populations". Applicants traverse the rejection based on lack of antecedent basis for "the antibody", as the antibody recited therein refers back to the recitation of "A blood analysis kit for performing an antibody test comprising". However, in the interest in advancing prosecution, Applicants have amended claim 42 to recite "to detect and identify an antibody which is the subject of the antibody test". It is respectfully submitted that such amendments will remove the rejection and Applicants respectfully request the rejection be withdrawn.

The Examiner further avers that in claims 46-48, recitation of "the populations" lacks antecedent basis. Applicants have amended claim 46 to specify a first and second population of reagent red cells, thereby, it is respectfully submitted, removing the grounds for the rejection which is respectfully requested.

Rejection Under 35 USC 102(b)

Claims 42-44 and 46-47 were rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Ullman (U.S. Pat. No. 4,584,277) for reasons of record in the prior rejection of the similar subject matter of claims 8-11. The Examiner avers Ullman teaches fluorescently labeled anti-blood group antigen antibodies and fluorescently labeled erythrocytes having blood group antigens thereon added simultaneously or sequentially to a sample of whole blood for multiparameter analysis of ABO blood type and isoantibodies (i.e. reverse blood typing) (see e.g. col. 3-4). A variety of combinations of parameters and suitable reagents are taught (see e.g. col. 3, Table 1). Suitable fluorescent labels are taught (e.g. col. 8-9); the Examiner avers that the reagents of the reference clearly anticipate those as instantly claimed.

Applicants have amended independent claims 42 and 46 to recite that the antibody test (claim 42) and the reverse ABO type (claim 46) is performed *in a single column*, and wherein the column *is subjected to visual or automated computerized imaging analysis* in order to determine the antibody (claim 42) or the reverse ABO type (claim 46). It is respectfully submitted that nothing in Ullman et al. discloses performance in a *single column* or subjects the test or type to *visual or automated*

computerized imaging analysis. The Ullman disclosure is directed to fluorescent detection analysis. Since claims 43 and 44 depend on amended claim 42, and since claim 47 depends upon amended claim 46, Applicants respectfully submit that the rejection is thereby overcome for all of claims 42-44 and 46-47 and so the same is respectfully requested.

Claims 16, 20, 22, 25-27, 29-34, 36-40, and 49-51 were rejected under 35 U.S.C. 102(b) as being anticipated by Yves [Lapierre] et al. (U.S. Pat. No. 5,338,689) for reasons of record in the prior rejection of the similar subject matter of claims 16, 20, 22 and 25-27. The Examiner avers that "a single test" as instantly claimed may be a multi-vessel technology.

Applicants have amended independent claims 16, 25, 31 and 36 to recite that the test is performed in a *single column.* Applicants respectfully submit that nothing in LaPierre teaches or suggests Applicants' methods of treating a population of reagent red blood cells with a dye in order to alter the color of one reagent cell population with respect to the other, and then using the reagent cell populations simultaneously in a *single column,* to determine ABO blood grouping of the sample, for example. Applicants therefore respectfully submit that since nothing in LaPierre teaches or suggests such discrimination of two distinct cell populations in a *single column,* the instant claims are patentable thereover and the rejection should respectfully be withdrawn. Since the dependent claims all depend on the amended independent claims it is respectfully requested that the rejection be withdrawn as to all the claims.

Claims 16, 20, 22, 25-27, 29-34, 36-40, and 49-51 were rejected under 35 U.S.C. 102(b) as being anticipated by Chachowski et al. (U.S. Pat. No. 5,552,064) for reasons of record in the prior rejection of the similar subject matter of claims 16, 20, 22, and 25-27; the Examiner notes that "a single test" as instantly claimed may be a multi-vessel technology.

Applicants have amended independent claims 16, 25, 31 and 36 to recite that the test is performed in a *single column*. Applicants respectfully submit that nothing in Chachowski et al. teaches or suggests Applicants' methods of treating a population of reagent red blood cells with a dye in order to alter the color of one reagent cell population with respect to the other, and then using the reagent cell populations simultaneously in a *single column*, to determine ABO blood grouping of the sample, for example. Applicants therefore respectfully submit that since nothing in LaPierre teaches or suggests such discrimination of two distinct cell populations in a *single column*, the instant claims are patentable thereover and the rejection should be withdrawn.

Applicants therefore respectfully submit that since nothing in Chachowski et al. teaches or suggests such discrimination of two distinct cell populations in a *single column*, the instant claims are patentable thereover and the rejection should be withdrawn. Since the dependent claims all depend on the amended independent claims it is respectfully requested that the rejection be withdrawn as to all the claims.

Claims 16, 20, 22, 23, and 25-51 were rejected under 35 U.S.C. 103(a) as being unpatentable over Chachowski et al. (U.S. Pat.No. 5,552,064) in view of Shen et al. (U.S. Pat. No. 5,594,808) for reasons of record in the prior rejection of the similar subject matter of claims 16, 20, 22, 23 and 25-28 wherein the Examiner avers that the teachings of Chachowski et al. are as set forth previously and admitted they differ from the invention as instantly claimed in not teaching an apparatus for interpretation of agglutination results; that Shen et al. teach an apparatus and method for classifying agglutination reactions in column agglutination devices; and that it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have used the device of Shen et al. for interpreting the results of Chachowski et al. because of the express suggestion in Shen et al. to do so. The Examiner thus concludes that the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Applicants have amended independent claims 16, 25, 31, 36, 42 and 46 to recite that the test is performed in a *single column,* as recited hereinabove. Applicants respectfully submit that nothing in Chachowski et al. either alone or when combined with Shen et al. teach the claimed detection of two cell populations in a *single column*. Chachowski et al. is directed to use of column agglutination technology (CAT) to detect presence of binding ligands, for example, blood group antigens or antibodies thereto, using separate forward and reverse or crosscheck tests, further employing a separation matrix. Shen et al. is directed to an automated computerized imaging system that is used to detect optically

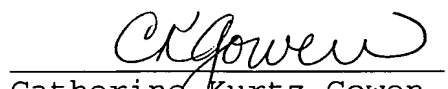
detectable binding complexes for example, carrier-bound antigens or antibody complexes and non-complexed carrier-bound antibodies and antigens, that form an agglutination pattern in microreaction vessels such as those used for column agglutination technology (CAT). Applicants respectfully submit that since nothing in Chachowski et al. when combined with Shen et al. teaches discrimination of two distinct cell populations in a *single column*, the instant claims are patentable thereover and the rejection should be withdrawn. Since the dependent claims all depend on the amended independent claims it is respectfully requested that the rejection be withdrawn as to all the claims.

The Examiner notes that the prior art of record and not relied upon is considered pertinent to Applicants' disclosure.

For the above-stated reasons and in light of Applicants' amendments made herein, it is respectfully submitted that the claims are patentable over the art cited. Applicants therefore request that the rejections be withdrawn and the claims be allowed.

Please charge the fees due in connection with the filing of this Amendment to Deposit Account No.10-0750/CDS-221/CKG in the name of Johnson & Johnson.

Respectfully submitted,



Catherine Kurtz Gowen
Attorney for Applicants
Registration No. 32,148

DATE: December 18, 2002

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933
Telephone No. 732-524-2681
Facsimile No. 732-524-2808

EXHIBIT A3

MARKED-UP VERSION OF CHANGES TO CLAIMS

16. [Thrice amended] A method of analyzing blood in a reverse test, comprising:

(a) admixing a sample of blood with reagent red blood cells bearing A antigen and with reagent red blood cells bearing B antigen
wherein such admixing is performed in a single [test] column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine ABO reverse type.

25. [Amended] A method of determining reverse ABO type [of] in a blood sample using two cell populations in a single [test] column, comprising:

(a) admixing a sample of blood with reagent red blood cells bearing A antigen and
reagent blood cells bearing B antigen, wherein such admixing is performed in a single [test] column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine reverse ABO type.

31. [Amended] A method of simultaneous blood antibody testing of a blood sample using two cell populations, comprising:

(a) admixing a sample of blood with a first group of reagent red blood cells bearing a first antigen and a second group of reagent red blood cells bearing a second antigen, wherein such

admixing is performed in a single [test] column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine reverse ABO type.

36. [Amended] A method of performing an antibody test on a sample of blood in a single [test] column comprising:

(a) admixing a sample of blood with reagent red blood cells bearing a first antigen and reagent red blood cells bearing a second antigen, wherein one of the populations of red blood cells is stained;

(b) allowing the admixture to agglutinate;

(b) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) detecting and identifying the antibody.

42. [Amended] A blood analysis kit for performing an antibody test in a single column comprising:

(a) a container having therein a first population of reagent red blood cells bearing a first antigen and a second population of reagent red blood cells bearing a second antigen, wherein one of the populations of reagent red blood cells is stained;

(b) reaction means for carrying out the antibody test; and

(c) instructions for performing the antibody test in order to detect and identify [the] an antibody which is the subject of the antibody test, wherein the column is subjected to visual or automated computerized imaging analysis.

46. [Amended] A blood analysis kit for performing a reverse ABO blood type in a single column comprising:

(a) a container having therein a first population of reagent red blood cells bearing group A antigen and a second population of reagent red blood cells bearing B antigen, wherein one of the populations of reagent red blood cells is stained;

(b) reaction means for carrying out the reverse ABO blood type; and

(c) instructions for performing the reverse ABO blood type, wherein the column is subjected to visual or automated computerized imaging analysis.

EXHIBIT A1

MARKED-UP VERSION OF CHANGES TO SPECIFICATION

At page 12, line 23, after "agglutination", insert --cross-hatched for color--.

At page 12, line 27, after "(orange)", insert --cross-hatched for color--.

At page 13, line 2, after "(green)", insert --cross-hatched for color--.

At page 13, line 6, after "(orange)", insert --cross-hatched for color--.

At page 13, line 9, after "agglutinates", insert --cross-hatched for color--.

At page 13, line 13, after "orange/green agglutinates", insert --cross-hatched for color--.

At page 13, line 24, after "column", insert --all cross-hatched for color--.

EXHIBIT A2

CLEAN VERSION OF CHANGES TO SPECIFICATION

Figure 2 show schematics of the expected results of simultaneous forward and reverse typing. Figure 2A shows that admixture of labeled A reagent RBCs and labeled anti-B with type A whole blood results in no agglutination (cross-hatched for color).

Figure 2B is a schematic representation of the admixture of labeled A reagent RBCs and labeled anti-B, with type B whole blood, resulting in agglutinates of B RBCs - with anti-B (green) and anti-A - A reagent cells (orange) (cross-hatched for color).

Figure 2C is a schematic representation of the admixture of labeled A reagent RBCs, and labeled anti-B, with type AB whole blood, resulting in agglutinates of AB RBC - anti-B (green) (cross-hatched for color).

Figure 2D is a schematic representation of the admixture of labeled A reagent RBCs and labeled anti-B, with type O whole blood, resulting in agglutinates of anti-A - A reagent cells (orange) (cross-hatched for color).

Figure 3 is a schematic representation of green agglutinates, orange agglutinates, and mixed orange/green agglutinates (cross-hatched for color), each of which will present different scatter on the green vs. orange max pixel spectra.

Figure 4 is a schematic representation of relative positions of orange agglutinates, green agglutinates, and

mixed orange/green agglutinates (cross-hatched for color) on the green vs. orange max pixel spectra.

Figure 6 is a schematic representation of visual detection of reverse testing of B serum in a CAT system. Labeled reagent A and B cells are admixed with B serum, resulting in brown agglutinates which, following centrifugation, are observed at the top of the gel column of the CAT system; the non-reacted labeled reagent B cells are observed at the bottom of the column (all cross-hatched for color).

EXHIBIT A4

CLEAN VERSION OF CHANGES TO CLAIMS

16. A method of analyzing blood in a reverse test, comprising:

(a) admixing a sample of blood with reagent red blood cells bearing A antigen and with reagent red blood cells bearing B antigen wherein such admixing is performed in a single column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine ABO reverse type.

25. A method of determining reverse ABO type in a blood sample using two cell populations in a single column, comprising:

(a) admixing a sample of blood with reagent red blood cells bearing A antigen and reagent blood cells bearing B antigen, wherein such admixing is performed in a single column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine reverse ABO type.

31. A method of simultaneous blood antibody testing of a blood sample using two cell populations, comprising:

(a) admixing a sample of blood with a first group of reagent red blood cells bearing a first antigen and a second group of reagent red blood cells bearing a second antigen, wherein such admixing is performed in a single column;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) analyzing the visual or automated computerized imaging analysis to determine reverse ABO type.

36. A method of performing an antibody test on a sample of blood in a single column comprising:

(a) admixing a sample of blood with reagent red blood cells bearing a first antigen and reagent red blood cells bearing a second antigen, wherein one of the populations of red blood cells is stained;

(b) allowing the admixture to agglutinate;

(c) subjecting the admixture to visual or automated computerized imaging analysis; and

(d) detecting and identifying the antibody.

42. A blood analysis kit for performing an antibody test in a single column comprising:

(a) a container having therein a first population of reagent red blood cells bearing a first antigen and a second population of reagent red blood cells bearing a second antigen, wherein one of the populations of reagent red blood cells is stained;

(b) reaction means for carrying out the antibody test; and

(c) instructions for performing the antibody test in order to detect and identify an antibody which is the subject of the antibody test, wherein the column is subjected to visual or automated computerized imaging analysis.

46. A blood analysis kit for performing a reverse ABO blood type in a single column comprising:

(a) a container having therein a first population of reagent red blood cells bearing group A antigen and a second population of reagent red blood cells bearing B antigen, wherein one of

the populations of reagent red blood cells is stained;

(b) reaction means for carrying out the reverse ABO blood type; and

(c) instructions for performing the reverse ABO blood type, wherein the column is subjected to visual or automated computerized imaging analysis.